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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/701,064	11/05/2003	H. William Bosch	029318-0978	6295

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EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
11/14/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/701,064	BOSCH ET AL.	
	Examiner	Art Unit	
	SUSAN TRAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-24,36-75 and 87-99* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-24,36-75 and 87-99* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/16/11;5/23/11;3/16/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

During the interview dated 11/08/10, it was indicated that the Restriction Requirement mailed 07/20/10 would be withdrawn. Hence, this Office Action:

Election/Restrictions

The Restriction Requirement mailed 07/20/10 is hereby withdrawn.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/02/10 has been entered.

Request for Correction of Inventorship

In view of the papers filed 07/13/09, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by the addition of Rajeev A. Jain, Jon Swanson, Robert Hontz, John G. Devane, Kenneth Ian Cumming,

Maurice Joseph Anthony Clancy, Janet Elizabeth Codd, and Gary G. Liversidge to the inventorship of the present application.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Claim Rejections - 35 USC § 103

Claims 1-15, 17-24, 40-75 and 87-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al. US 5,510,118, in view of Stamm et al. WO 98/31360 A1.

Bosch teaches a nanoparticulate therapeutic composition comprising of 99.9-10% by weight of a crystalline drug substance, and from about 0.1 to about 90% by weight of a non-crosslinked surface modifier adsorbed on the surface of the drug substance. See Abstract; and claim 1. The nanoparticulate has an effective average particle size of less than about 400 nm (abstract; column 6, lines 36-54; and claim 1). Suitable drug substance includes anti-diabetic agents (column 5, line 5). The claimed surface modifiers are disclosed in column 5, lines 45 through column 6, lines 1-5. Surface modifier can be used in combination of two or more (column 6, lines 10-12). Bosch further teaches a method for preparing the dispersible particle comprising dispersing a drug substance in a liquid dispersion that contains surface modifier to form a premix, homogenizing the premix, and subjecting the premix to grinding media (columns 7-8; examples; and claims). The obtained dispersion of surface modified drug

nanoparticles is combined with pharmaceutical excipient to form pharmaceutical formulation for oral, rectal, injection administration, and the like (column 8, lines 40 through column 9, lines 1-17). Bosch further teaches that the surface modifier is essentially free of intermolecular crosslinkages (column 6, lines 34-35).

Bosh does not explicitly teach the claimed active, such as glipizide.

Stamm teaches a composition having high bioavailability comprising micronized glipizide as active agent suspended in a solution containing surfactant (page 5, lines 32-38; examples 1 and 6). Stamm further teaches active agent in micronized form having particle size below 20 μm. Thus, it would have been obvious to one of ordinary skill in the art to select glipizide as an active agent because Stamm teaches that glipizide is a well-known insoluble drug, and that the need to improve dissolution and bioavailability of glipizide is well known in the art, and because Bosh teaches a formulation suitable for improving bioavailability of a wide variety of active agents including anti-diabetic agents.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al., in view of Stamm et al. and Baralle et al. GB 2316316.

Bosch is relied upon for the reasons stated above. The references do not teach the second population of particle having different particle distribution from the particle distribution of (a). However, bimodal particle distribution is known in pharmaceutical art. Baralle teaches a liquid composition comprising bimodal particle size distribution suitable for parenteral administration (abstract; page 3, lines 23-32; and page 7, lines 3 through page 8, lines 1-23). Accordingly, depending in the release profile desired, the

skilled artisan would have been motivated to modify the formulation of Bosch to include a bimodal particle distribution in view of the teachings of Baralle. This is because Baralle teaches a bimodal particle distribution is known in pharmaceutical art, because Baralle teaches a bimodal particle distribution that exhibits a useful sustained release profile that is free of serious side-effects (pages 3-4).

Claims 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al., in view of Stamm et al. and Lo et al. 4,389,397.

Bosch is relied upon for the reason stated above. The references do not explicitly teach the viscosity of the liquid dosage form.

Lo teaches a low water solubility drug is preferably formulated in liquid dosage form having low viscosity to achieve excellent stability and syringability (abstract; and column 4, lines 10-17). Thus, it would have been obvious to one of ordinary skill in the art to prepare a low viscous liquid dosage form in view of the teachings of Bosch and Lo to obtain a stable liquid dosage form suitable for water-insoluble drug. This is because Lo teaches Lo teaches liquid dosage form having high viscosity will cause precipitation, irritation and tissue damage at the injection site (column 1, lines 25-29), because Lo teaches a low viscosity liquid dosage form overcomes the disadvantages in the prior arts and exhibits excellent syringability (ID).

Claims 91-99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al. US 5,510,118, in view of Stamm et al. WO 98/31360 A1 and Eoga et al. US 5,939,091.

Bosch is relied upon for the reasons stated above. Bosch does not teach the claimed fast melt tablet.

Eoga teaches a fast melt tablet comprising nanoparticle of poorly water soluble active agent (column 6, lines 5-13).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a fast melt tablet that includes a nanoparticulate glipizide in view of the teachings of Eoga. This is because Eoga teaches a fast melt tablet suitable for the delivery of an antidiabetic agent (column 5, line 66), and because Eoga teaches the incorporation of a nanoparticulate water-insoluble active agent in a fast melt tablet dosage form is known in the art.

Response to the Response filed 08/10/11

The Declaration under 37 CFR 1.132 filed 08/10/11 is insufficient to overcome the 1103(a) rejections of record as set forth in the last Office action for the following reasons:

1) it refer(s) only to the system described in the above referenced application and not to the individual claims of the application. Thus, there is no showing that the objective evidence of nonobviousness is commensurate in scope with the claims. See MPEP § 716;

2) USPN 7,217,431 is not cited in the rejections;

3) the Declaration citing ketoprofen, which is not the claimed bioactive agent; and

4) the teachings in 7,217,431 does not include the use of surfactant in combination with nanoparticulate in order to improve bioavailability.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Response to Arguments

Applicant's arguments filed 08/10/11 have been fully considered but they are not persuasive.

Applicant argues that Bosch's teaching of a genus does not render the claimed species obvious (see Remarks filed 08/10/11 at pages 23-24).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Bosch is cited in view of Stamm for the specific teaching of glipizide. Stamm teaches micronized glipizide as active agent suspended in a solution containing surfactant will result in a composition having high bioavailability (page 5, lines 32-38; examples 1 and 6). Because Bosch teaches a composition that is useful for a wide variety of active agents that include an antidiabetic agent, it would have been obvious to one of ordinary

skill in the art to select glipizide as one of the antidiabetic agent because Stamm teaches that there is the need to improve dissolution and bioavailability of glipizide.

Applicant cited USPN 7,217,431 in the 1.132 Declaration to show that improved bioavailability is not a predictable result of forming a nanoparticulate active agent composition.

However, as discussed above, it is noted that US 7,217,431 teaches away from using surface active agent on the surface of a nanoparticulate to improve the bioavailability of the active agent.

Accordingly, for at least the above reasons, the 103(a) rejections of record are maintained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1615